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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,712	11/03/2005	Herman Augustinus De Kock	TIP-0072USPCT	2964
27777	7590	03/30/2009	EXAMINER	
PHILIP S. JOHNSON JOHNSON & JOHNSON ONE JOHNSON & JOHNSON PLAZA NEW BRUNSWICK, NJ 08933-7003			BIANCHI, KRISTIN A	
			ART UNIT	PAPER NUMBER
			1626	
			MAIL DATE	DELIVERY MODE
			03/30/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/555,712	DE KOCK ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	KRISTIN BIANCHI	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 December 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-23 and 26-31 is/are pending in the application.
- 4a) Of the above claim(s) 26 and 28-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 November 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>05/07/2008 and 05/07/2008</u> .                               | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1-23 and 26-31 are pending in the instant application. Claims 26 and 28-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected subject matter. The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations. In addition, a reference which anticipates one group would not render obvious the other. Claims 1-23 and 27 are rejected.

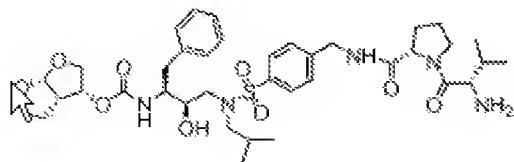
#### ***Information Disclosure Statements***

The information disclosure statement filed on May 7, 2008 which consisted of one page was considered and a signed copy of form 1449 is enclosed herewith. The other information disclosure statement filed on May 7, 2008 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance of some of the references (i.e., (1) Ash M. et al., (2) Atherton, E. et al., (3) "Drug Bioavailability: Estimation of Solubility, Permeability, Absorption and Bioavailability," (4) McCutcheon's Emulsifiers and Detergents, (5) "Tensid-Taschenbuch," and (6) WO 99/67278), therefore, those six references have been stricken out in the signed copy of the 1449 form or were not considered. Also, the above listed references do not contain pages with relevant information (i.e., just the table of contents, title pages or a list of US Family Members are submitted).

#### ***Election/Restrictions***

Art Unit: 1626

Applicant's election of Group III, claims 1-23 and 27, and the species disclosed in



claim 21 or

in the response filed December 24,

2008 has been acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is maintained.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/67254 (Erickson et al.) in view of US 2002/0049164 (Demuth et al.) further

Art Unit: 1626

in view of Meester et al. (Immunology Today, Vol. 20 No. 8, August 1999, pages 367-375) and WO 99/33792 (Hale et al.).

***Determining the scope and contents of the prior art***

Erickson et al. discloses compounds of formula (I) which are retroviral protease-inhibiting (abstract), such as the first compound listed in Table 4 on page 57.

Demuth et al. discloses prodrug compounds of inhibitors of dipeptidyl peptidase IV (DP IV) which have the general formula A-B-C wherein A is an amino acid, B is a chemical bond between A or C or is an amino acid and C is a stable inhibitor of DP IV (abstract). Demuth et al. also discloses that when a prodrug compound of formula A-B-C interacts with a DP IV molecule, it is cleaved by the enzyme into the groups A-B and the inhibitor C ([0017]).

Hale et al. discloses prodrugs of a class of sulfonamides which are HIV aspartyl protease inhibitors (abstract).

Meester et al. discloses (page 367, 1<sup>st</sup> paragraph) that CD26 is identical to dipeptidyl-peptidase IV and has a high selectivity for peptides with a proline or alanine at the second position and cleaves off dipeptides at the N-terminus of such peptides.

***Ascertaining the differences between the prior art and the claims at issue***

Erickson et al. does not disclose peptidyl prodrug derivatives of the compounds of formula (I).

Demuth et al. does not disclose compounds of formula (I) of the instant claims minus the amino acid groups or (Y-X)<sub>n</sub> as the inhibitor compound or C in the formula A-B-C of the prodrug compounds.

Hale et al. does not disclose the same type of prodrugs (i.e. peptidyl prodrug derivatives) or compounds of formula (I) of the instant claims.

Meester et al. does not disclose the prodrugs of the instant claims.

***Establishing a prima facie case of obviousness***

Since it was known in the art at the time of the invention that prodrugs of HIV aspartyl protease inhibitors have been successfully made (i.e., Hale et al.), that peptidyl prodrug derivatives of compounds are cleavable by DP IV and are useful (i.e., Demuth et al., [0017]) and that CD26 has a high selectivity for peptides with a proline or alanine at the second position (i.e., Meester et al.), it would have been obvious to one of ordinary skill to take the compounds or inhibitors of HIV aspartyl protease disclosed in Erickson et al., make peptidyl prodrug derivatives

Art Unit: 1626

wherein the amino acid in the second position is proline or alanine and arrive at a prodrug of the instant claims with a reasonable expectation of success for obtaining a prodrug with the same activity. It also would have been obvious to one of ordinary skill to experiment with the number and type of amino acid groups added to the end of the compounds or (Y-X)<sub>n</sub> as a way to alter and perhaps improve (i.e., for pharmacological use) the properties of the compounds (i.e., the solubility, hydrophobicity, degradation rate, etc.).

The motivation would have been to make additional prodrugs of compounds which are well known to inhibit HIV aspartyl protease and are useful as pharmaceuticals.

Thus, a *prima facie* case of obviousness has been established.

### **Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIN BIANCHI whose telephone number is (571)270-5232. The examiner can normally be reached on Mon-Fri 7am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1626

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed/  
Primary Examiner, Art Unit 1626

Kristin Bianchi  
Examiner  
Art Unit 1626

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